

We claim: .

1. A hirudin precursor, comprising a signal sequence selected from signal sequences of an outer membrane protein of *Serratia marcescens*, an oprF protein of *Pseudomonas fluorescens*, a lamB protein of *Escherichia coli*, and a fumarate reductase of *Shewanella putrifaciens*, wherein aa<sub>x</sub>-hirudin is attached at the C-terminal of said signal sequence, wherein aa<sub>x</sub> represents an amino acid.
2. The precursor of claim 1, where said signal sequence is selected from a signal sequence of an outer membrane protein of *Serratia marcescens*, and a fumarate reductase of *Shewanella putrifaciens*.
3. The precursor of claim 1, wherein aa<sub>x</sub> is leucine.
4. A process for preparing aa<sub>x</sub>-hirudin, wherein aa<sub>x</sub> is an amino acid, comprising:
  - (a) preparing a hirudin precursor comprising a signal sequence selected from signal sequences of an outer membrane protein of *Serratia marcescens*, an oprF protein of *Pseudomonas fluorescens*, a lamB protein of *Escherichia coli*, and a fumarate reductase of *Shewanella putrifaciens*, wherein aa<sub>x</sub>-hirudin is attached at the C-terminal of said signal sequence,
  - (b) preparing an expression plasmid comprising a DNA sequence coding for said hirudin precursor;
  - (c) expressing said expression plasmid from (b) in a suitable *E. coli*, wherein said *E. coli* is in a culture medium;
  - (d) secreting said selected hirudin precursor from said *E. coli*, wherein said selected hirudin precursor is simultaneously processed; and
  - (e) isolating aa<sub>x</sub>-hirudin from the culture medium.
5. The process of claim 1, wherein aa<sub>x</sub> is leucine.

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6. A process for selecting a suitable signal peptide for secretory expression of a desired protein in *E. coli*, comprising:

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- (a) expressing in *E. coli* in culture medium, hirudin or a hirudin derivative which has antithrombotic activity, and which has a defined amino acid, aa<sub>x</sub>, at its N terminus, wherein said amino acid aa<sub>x</sub> is connected via its N-terminal to a signal peptide to be tested;
  - (b) determining expression rate by measuring said protein activity in the culture supernatant;
  - (c) repeating steps (a) and (b) with various signal peptides;
  - (d) selecting said suitable signal peptide by comparing the expression rates represented by the hirudin antithrombotic activity found in step (b).

7. The process of claim 6, wherein aa<sub>x</sub> is leucine.

8. The process of claim 6, further comprising expressing said suitable signal peptide and the desired protein in *E. coli* via a nucleic acid construct, wherein expression of the desired protein and said suitable signal peptide occurs with simultaneous elimination of said suitable signal peptide.

9. The process of ~~any one of claims 6, 7, or 8~~, wherein the desired protein is ~~hirudin~~.

10. A process of efficiently producing a desired protein comprising:

- (a) selecting a suitable signal peptide according to the process of claim 6;
- (b) preparing a nucleic acid construct coding for a precursor protein consisting of the suitable signal peptide from step (a) and the desired protein; and
- (c) expressing the nucleic acid construct of step (b) in *E. coli*, wherein the selected suitable signal peptide is simultaneously eliminated.

11. The process of claim 10, further comprising isolating the desired protein from culture supernatant.
12. The process of claim 10 wherein aa<sub>x</sub> is leucine.
13. The process of claim 10, wherein said nucleic acid construct has a sequence coding for said selected signal peptide selected from an outer membrane protein of *Serratia marcescens*, an oprF protein of *Pseudomonas fluorescens*, a lamB protein of *Escherichia coli*, and a fumarate reductase of *Shewanella putrifaciens*.
14. The process of any one of claims 10, 11, 12, or 13, wherein the desired protein is hirudin.